pentaerythritol tetranitrate, erythrityl tetranitrate, sodium nitroprusside, 3-morpholinosydnonimine, molsidomine, S-nitroso-N-acetylpenicillamine, S-nitrosoglutathione, N-hydroxy-L-arginine, S,S-dinitrosodithiol and NO gas.

80. The method of claim 70 wherein the agent which augments action of cGMP is glyceryl trinitrate.--

**REMARKS**

Claims 35-40, 45-51 and 53-59 are pending in the instant application. Claims 35-40, 45-51 and 53-59 have been rejected. Claims 35-40, 45-51 and 53-59 have been canceled and new claims 60-80 have been added. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

The rejection of claims 35-40, 45-51 and 53-59 under 35 U.S.C. § 103(a) as being unpatentable over both Anfossi et al. and Maurice et al. in view of Snyder et al., Gozes et al. and Stamler et al. has been maintained. The Examiner suggests that the claim limitation "while decreasing or eliminating pain associated with erection" does not patentably distinguish the claims from the cited prior art since the claims are directed to the "ultimate utility (erectile dysfunction)" set forth in the prior art.

Accordingly, in an earnest effort to advance the prosecution and to clarify the "ultimate utility" of the present invention which is patentably distinguishable from the prior art teachings, Applicants have canceled the pending claims, representing the invention in new claims 60-80. New claims 60-80 are drawn to a method of decreasing pain associated with use of prostaglandins for treatment of erectile tissue dysfunction comprising administering to a subject at least one agent that produces NO and/or augments action of cGMP in nociceptive tissue in close proximity to engorgeable genital tissue. Support for these claims is found throughout the specification and in particular at page 5, lines 4-5, page 9, lines 3-4, page 10, lines 25-27, page 13, lines 17-18, the case studies presented at pages 16-18, page 18, lines 16-21, page 19, and the claims as originally filed. Thus, no new matter is presented by this amendment.

When prostaglandins are administered by any route, particularly via intracavernous injection or topically as a cream, for treatment of erectile or sexual dysfunction, utility of the prostaglandin treatment is limited by pain. For example, with respect to treatment of erectile dysfunction, the erectile response is actually decreased as the pain increases. Thus, a method for decreasing pain associated with prostaglandin treatment of erectile

dysfunction or sexual dysfunction actually enhances the efficacy and therefore the utility of prostaglandin treatment for such dysfunction.

There is no teaching or suggestion of a method for decreasing pain associated with prostaglandin treatment, as now claimed, in the combination of cited prior art references.

The primary references cited in the rejection relate solely to platelets and their aggregation. Further, these references focus on the effects of agents on **intra**platelet cAMP and cGMP levels, a measurement irrelevant and not predictive of the ability of such agents to decrease pain associated with prostaglandin treatment in engorgeable genital tissue systems and tissue systems adjacent thereto.

The cited secondary references fail to remedy the deficiencies in the primary references as these references have been cited for their teachings relating to erectile dysfunction only. There is no teaching or suggestion in any of these secondary references relating to use of agents that produce NO and/or augment action of cGMP in nociceptive tissue in close proximity to engorgeable genital tissue to decrease pain associated with use of prostaglandins for erectile tissue dysfunction.

Accordingly, the cited combination of references fails to teach or suggest all the limitations of the claims as amended.

Further, as taught at page 11, lines 19-22, of the specification, references such as Snyder et al. concerning reversing priapism with NO synthase inhibitors, as well as studies on analgesics and NO, actually provide an expectation of **increased** pain with administration of such agents. Thus, the cited combination of prior art actually teaches away from any reasonable expectation of success that administration of these agents will decrease pain associated with use of prostaglandins for erectile tissue dysfunction. Further, the ultimate utility of the present invention, to decrease pain associated with use of prostaglandins for erectile tissue dysfunction, can not be inherent in light of the cited prior art teachings since one of skill in the art would not have recognized the ability of the agents to decrease pain, as claimed in the method of the present invention, from the cited combination of prior art. See MPEP § 2112.

The invention as now claimed is clearly neither taught nor suggested by, nor inherent in, the combination of prior art references cited in this rejection. Thus, the claimed invention cannot be obvious over these teachings.

Withdrawal of this rejection under 35 U.S.C. § 103(a) is respectfully requested in light of the amendments to the claims and the above arguments.

**CONCLUSION**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto, on page 10, is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

Date: **April 5, 2001**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053
(856) 810-1515

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Claims 35-40, 45-51 and 53-59 have been canceled.

Claims 60-80 have been added.